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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,784	04/14/2004	Karen Uhlmann	3035-101	4952

46002 7590 02/16/2007

JOYCE VON NATZMER
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EXAMINER	
SHAW, AMANDA MARIE	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
02/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

Interview Summary	Application No.	Applicant(s)	
	10/823,784	UHLMANN ET AL.	
	Examiner	Art Unit	
	Amanda M. Shaw	1634	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Amanda M. Shaw*.

(2) *Ram Shukla*.

(3)*Joyce von Natzmer*.

(4)_____.

Date of Interview: *12 February 2007*.

Type: a)☐ Telephonic b)☐ Video Conference
c)☒ Personal [copy given to: 1)☐ applicant 2)☒ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☒ No.
If Yes, brief description: _____.

Claim(s) discussed: *1 and 34*.

Identification of prior art discussed: *The Nyren et al (US Patent 6258568) and Eads et al (Nucleic Acids Research 2000) references were discussed*.

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *The applicants wished to discuss the rejections made under 35 USC 103. A draft of proposed claim amendments faxed to the examiner on 2/10/2007 was also discussed (see attachement). The applicants also wanted to discuss the rejection of claim 34 made under 35 USC 112 2nd paragraph. Suggestions were made regarding claim amendments*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)
In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Draft

Joyce v. Natzmer
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FACSIMILE COVER SHEET

To:	**Examiner Shaw**
Cc:	
Company:	USPTO Art Unit 1634
Fax:	(571)273-8668
From:	Joyce von Natzmer
Re:	**Interview on 2/12/07 at 1:30 pm; Appl. No. 10/823,784**

Date: February 10, 2007

Pages (including this cover sheet): 10

Dear Examiner Shaw

Thank you for granting me a personal interview in connection with the subject application on Monday, February 12, 2007 at 1:30 pm. As discussed on the phone, please find attached claim amendments and "talking points" (page 9) for our interview.

I am looking forward to discussing this application with you on Monday.

Cordially,

Joyce v. Natzmer

ENTER

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Karen UHLMANN et al	Confirmation No. 4952
Appln. No.: **10/823,784**	
Filed: April 14, 2004	Examiner: Amanda M. Shaw
For: **METHOD OF DETECTING EPIGENETIC BIOMARKERS.....**	Art Unit: 1634
	ATTY. DKT: 3035-101

Draft Claims for Interview on 2/12/07

Claims not containing any proposed amendments are shown in italics

1. (Currently Amended) A method for detecting the methylation status of a nucleotide at a predetermined position in a nucleic acid molecule comprising:

(a) treating a sample comprising said nucleic acid molecule in an aqueous solution with an agent suitable for the conversion of said nucleotide if present in

(i) methylated form; or

(ii) non-methylated form

to pair with a nucleotide normally not pairing with said nucleotide prior to conversion;

(b) amplifying said nucleic acid molecule treated with said agent to generate an amplified nucleic acid molecule;

(c) real-time sequencing said in (b) amplified nucleic acid molecule; and

(d) detecting whether said nucleotide is methylated or not methylated at said predetermined position in the sample.

DO NOT enter

2. *(Original) The method of claim 1 wherein said sample is derived from a tissue, a body fluid or stool.*

3. *(Original) The method of claim 2 wherein said tissue is a tumor tissue, neurodegenerative tissue or a tissue affected with another neurological disorder.*

4. *(Previously Presented) The method of claim 1 wherein said nucleic acid molecule is a DNA molecule or an RNA molecule.*

5. *(Previously Presented) The method of claim 1 wherein in (b) the nucleic acid molecule is amplified via LCR or PCR.*

6. *(Original) The method of claim 5 wherein one amplification primer is detectably labeled.*

7. *(Previously Presented) The method of claim 6 wherein said amplification primer is labeled with (a) biotin, (b) avidin, (c) streptavidin or (d) a derivative of (a), (b) or (c) or a magnetic bead.*

8. (Previously Presented) The method of claim 1 wherein said methylated nucleotide is ~~an adenine, guanine or~~ a cytosine.

9. *(Previously Presented) The method of claim 1 wherein said real-time sequencing comprises:*

(a) hybridization of a sequencing primer to said amplified nucleic acid molecule in single-stranded form;

(b) addition of a DNA polymerase, a ATP sulfurylase, a luciferase, an apyrase, adenosine-phosophosulfate (APS) and luciferin;

(c) sequential addition of all four different dNTPs;

(d) detection of a luminescent signal wherein an intensity of the luminescent signal is correlated with the incorporation of a specific nucleotide at a specific position in the nucleic acid molecule and wherein the intensity of said signal is indicative of the methylation status of said nucleotide at said predetermined position.

10. (Previously Presented) The method of claim 1, wherein said nucleotide is methylated and further comprising quantifying ~~the methylated nucleotides~~ said nucleotide.

11. (Previously Presented) The method of claim 1 wherein said agent suitable for the conversion of said nucleotide to pair with nucleotide normally not pairing with said nucleotide is a bisulfite, preferably sodium bisulfite.

12. (Previously Presented) A method for the diagnosis of a pathological condition or the predisposition for a pathological condition comprising detection of the methylation status of a nucleotide at a predetermined position in a nucleic acid molecule comprising:

(a) treating a sample comprising said nucleic acid molecule in an aqueous solution with an agent suitable for the conversion of said nucleotide if present in

(i) methylated form; or

(ii) non-methylated form

to pair with a nucleotide normally not pairing with a said nucleotide prior to conversion;

(b) amplifying said nucleic acid molecule treated with said agent to generate an amplified nucleic acid molecule;

(c) real-time sequencing said amplified nucleic acid molecule; and

(d) detecting whether said nucleotide is methylated or not methylated at said predetermined position in the sample wherein a methylated or a not methylated nucleotide is indicative of a pathological condition or the predisposition for said pathological condition.

13. (Currently Amended) The method of claim 12 wherein said pathological condition is cancer~~, a neurodegenerative disease or another neurological disorder~~.

14. (Original) The method of claim 13 wherein said cancer is a primary tumor, a metastasis or a residual tumor.

15. (Original) The method of claim 14 wherein said primary tumor is a glioma.

16. (Previously Presented) The method of claim 15 wherein said glioma is an astrocytoma, oligodendroglioma, an oligoastrocytoma, a glioblastoma, or a pilocytic astrocytoma.

17. (Original) The method of claim 13 wherein said neurodegenerative

disease is Alzheimer's disease, Parkinson disease, Huntington disease, or Rett-Syndrome.

18. (Original) The method of claim 13 wherein said neurological disorder is Prader-Willi-Syndrom, Angelman-Syndrome, Fragile-X-Syndrome, or ATR-X-Syndrome.

19. (Previously Presented) The method of claim 12 wherein said nucleic acid molecule is a DNA molecule or an RNA molecule.

20. (Previously Presented) The method of claim 12 wherein in (b) the nucleic acid molecule is amplified via LCR or PCR.

21. (Original) The method of claim 20 wherein one amplification primer is detectably labeled.

22. (Previously Presented) The method of claim 21 wherein said amplification primer is labeled with (a) biotin, (b) avidin, (c) streptavidin or (d) a derivative of (a), (b or (c) or a magnetic bead.

23. (Previously Presented) The method of claim 12 wherein said methylated nucleotide is an adenine, guanine or a cytosine.

24. (Previously Presented) The method of claim 12 wherein said real-time sequencing comprises:

(a) hybridization of a sequencing primer to said amplified nucleic acid molecule in single-stranded form;

(b) addition of a DNA polymerase, a ATP sulfurylase a luciferase, an Apyrase, adenosine-phosphosulfate (APS) and luciferin;

(c) sequential addition of all four different dNTP's

(d) detection of a luminescent signal wherein the intensity of the luminescent signal is correlated with the incorporation of a specific nucleotide at a specific position in the nucleic acid molecule and wherein the intensity of said signal is indicative of the methylation status of said nucleotide at said predetermined position.

25. (Previously Presented) The method of claim 12 further comprising quantifying the methylated nucleotides.

26. (Previously Presented) The method of claim 12 wherein said agent suitable for the conversion of said nucleotide to pair with a nucleotide normally not pairing with said nucleotide is a bisulfite, preferably sodium bisulfite.

27. (Previously Presented) The method of claim 1 wherein said method is a high-throughput method.

28. (Previously Presented) The method of claim 12 wherein said sample is derived from tissue, a body fluid or stool.

29. (Previously Presented) The method of claim 28 wherein said body fluid is blood, serum or urine.

30. (Previously Presented) The method of claim 1 wherein said nucleotide is a cytosine and is part of one of the following sequences: CpG, CpNpG or CpNpN.

31. (Previously Presented) The method of claim 1, wherein the methylation status of more than one predetermined nucleotide is detected and a number of samples are analyzed at the same time.

32. (Currently Amended) A method for generating new nucleotide pairing partners upon amplification of at least one nucleic acid molecule for the detection of the methylation status of nucleotides of said nucleic acid molecule, said method comprising:

a. providing said at least one nucleic acid molecule;

b. treating said nucleic acid molecule with an agent suitable for conversion of a nucleotide if present in methylated form or non-methylated form to pair with nucleotide pairing partners normally not pairing with said nucleotide prior to conversion;

c. amplifying said nucleic acid molecule to ~~produce an amplification product comprising~~ generate said new nucleotide pairing partners normally not pairing with said nucleotide prior to conversion;

d. real-time sequencing said ~~amplification product~~ in c. amplified nucleic acid molecule;

e.determining the amount of said nucleotide pairing with said new nucleotide pairing partners ~~in said amplification product~~ to detect the methylation status of nucleotides of said nucleic acid molecule.

33. (Previously Presented) The method of claim 1, wherein the methylation status of more than one predetermined nucleotide is determined.

34. (Previously Presented) The method of claim 10, wherein an allele frequency of 5% can be detected.

35. (New) The method of claim 1

wherein said methylated nucleotide is an adenine or guanine.

36. (New) The method of claim 12 wherein said pathological condition a neurodegenerative disease or another neurological disorder.

Topics for discussion during interview on 2/12/07

Time: 1:30 pm

Remsen Building

All rejections of the Office Action of 11/15/06 with particular emphasis on:

35 U.S.C. §103 rejection

- The difference between Eads' disclosure of, on the one hand, the MethyLight method and, on the other hand, genomic bisulfite sequencing and the claimed invention.

35 U.S.C. §112, second paragraph rejection of claim 34

- requirement for "active process step" under 2. of 11/15/06 Office Action.
- lack of evidence argument made under 3. of 11/15/06 Office Action in view of 7/14/06 response, page 10 and specification page 24, first full paragraph.

Inherency rejection of claim 34

- rationale provided in final Office Action of 11/15/06 in the paragraph spanning pages 19/20 of 11/15/06 Office Action (see also page 14 of 11/15/07 Office Action and original inherency rejection on page 14 of 7/26/06 Office Action).

Claim 32

- proposed claim amendment to overcome the issues raised on pages 12 and 19 of 11/15/06 Office Action.